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10/542,997	07/21/2005	Kazuhiro Ohkouchi	084437-0173	7856

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EXAMINER	
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1615	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,997	OHKOUCHI ET AL.	
	Examiner	Art Unit	
	BETHANY BARHAM	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summary

Applicant's Response and Claim Amendments filed on 4/24/09 is acknowledged. Claims 14-20 are pending.

Due to Applicant's Claim Amendments the previous rejections of record are hereby withdrawn.

NEW REJECTIONS

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 01/82875 ('875, as cited by Applicant) in view of US 5,547,683 ('683).

The instant claims are drawn to a method of producing a coated preparation, which comprises coating a core with an aqueous dispersion of pioglitazone hydrochloride comprising a coating material selected from the group consisting of

(a) hydroxypropyl cellulose, wherein (i) a 5%(w/v) aqueous solution of which cellulose has a viscosity of 24 mPa.s at 20°C and/or (ii) a 2%(w/v) aqueous solution of which cellulose has a viscosity of 3.0-5.9 mPa.s at 20°C;

(b) hydroxypropyl cellulose, wherein (i) a 5%(w/v) aqueous solution of which cellulose has a viscosity of 8 mPa.s at 20°C and/or (ii) a 2%(w/v) aqueous solution of which cellulose has a viscosity of 2.0-2.9 mPa.s at 20°C; and

(c) polyvinyl alcohol-polyethylene glycol graft copolymer whose 5%(w/v) aqueous solution has a viscosity of not more than 35 mPa.s at 20°C,

wherein the core comprises an active ingredient.

- '875 teaches in claim 8, a method for producing a combined formulation of pioglitazone HCl and metformin comprising a) forming a core of the metformin and b) depositing a layer of pioglitazone hydrochloride on at least a portion of the surface of said core (pg. 2, lines 20-30; pg. 3, lines 3-6). '875 teaches that the shell layer comprising the pioglitazone HCl is formed via solvent removal process (pg. 7, line 31-pg. 8, line 2) and that cellulosic polymers and polyvinyl alcohol are taught as a biodegradable material further included in the coating of the dosage form (pg. 7, lines 21-27) (according to the limitations of claim 14-16 and 20).
- '875 defines "metformin" to mean the base compound as well as its pharmaceutically acceptable salts, including metformin hydrochloride (pg. 1, lines 27-29) (according to the limitation of claim 17).
- '875 does not teach the specific cellulosic polymers instant claimed.
- '683 teaches coating a granule with 5% HPC-SSL (Example 1) and that low viscosity polymers of HPC (such as HPC-SL and HPC-SSL) are preferably used

since their binding power is not to high and allows easy control of particles (col. 4, lines 24-33).

- The prior art teaches the same method of coating a dosage form with the same composition as instant claimed and it is therefore assumed in the absence of evidence otherwise to have the same dissolution improvement (as required by the limitation of claim 20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the low viscosity cellulosic polymer HPC-SSL or HPC-SL of '683 into the formulation of '875 with predictable results. A skilled artisan would know how to make such a substitution of one generic cellulosic polymer of '875 for the specific HPC-SSL or HPC-SL of '683 and would be especially motivated to make such a substitution since '683 teaches that the low viscosity HPC (such as HPC-SSL) is preferred since the binding power is not to high as a high binding power leads to gelation which is disadvantageous (col. 4, lines 27-30 and 45-49).

Claims 14-17 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2004/0106660 ('660) (which has priority to 09/20/2002) as cited by Applicant.

- '660 teaches a combined formulation of pioglitazone HCl and metformin comprising a) forming a core of the metformin HCl and b) depositing coating layer of pioglitazone hydrochloride and polymer in water on the surface of said core (abstract, [0016], Examples 1-2) (according to the limitations of claims 14-17 and 20).

- '660 teaches that the binder (hydroxypropylmethyl cellulose or hydroxypropylcellulose) is included in the composition in an amount of 1-15% by weight of the total dosage form ([0042] table) (meeting the limitations of claim 3).
- '660 teaches that the coating is formed via spraying a suspension of comprising the pioglitazone HCl and hydroxypropylmethylcellulose or hydroxypropylcellulose in purified water ([0035, 0023], [0042] table; and Examples 1-2).
- '660 does not teach the specific cellulosic polymers instant claimed.
- '683 teaches coating a granule with 5% HPC-SSL (Example 1) and that low viscosity polymers of HPC (such as HPC-SL and HPC-SSL) are preferably used since their binding power is not to high and allows easy control of particles (col. 4, lines 24-33). According to the instant specification and originally filed claims HPC-SL and HPC-SSL meet the % aqueous solution and viscosity as instant claimed (pg. 5, line 30-pg. 6, line 3).
- The prior art teaches the same method of coating a dosage form with the same composition as instant claimed and it is therefore assumed in the absence of evidence otherwise to have the same dissolution improvement (as required by the limitation of claim 20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the low viscosity cellulosic polymer HPC-SSL or HPC-SL of '683 into the formulation of '660 with predictable results. A skilled artisan would know how to make such a substitution of one generic HPC of '660 for the specific HPC-SSL or HPC-SL of '683 and would be especially motivated to make such a substitution since '683

teaches that the low viscosity HPC (such as HPC-SSL) is preferred since the binding power is not to high.

Claims 14 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0060488 ('488) in view of 'US 5,547,683 ('683).

- Example 1 teaches pioglitazone HCl combined with an aqueous solution with hydoxypropylcellulose (according to the limitation of claim 14 and 20). '488 teaches that oral preparation for the actives can be prepared by mixing separately and that such binders like hydroxypropylmethylcellulose or hydroxypropylcellulose can be used in the core or in the coating [0154, 0157-0158].
- '488 teaches a combination of an insulin sensitizer preferably pioglitazone HCl with a HMG-CoA reductase inhibitor like a statin compound such as pravastatin, simvastatin, atorvastatin, etc [0009, 0023, 0025-0026, 0123, 0139, 0145-0148] (according to claims 18-19).
- '683 teaches coating a granule with 5% HPC-SSL (Example 1) and that low viscosity polymers of HPC (such as HPC-SL and HPC-SSL) are preferably used since their binding power is not to high and allows easy control of particles (col. 4, lines 24-33).
- The prior art teaches the same method of coating a dosage form with the same composition as instant claimed and it is therefore assumed in the absence of evidence otherwise to have the same dissolution improvement (as required by the limitation of claim 20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the low viscosity cellulosic polymer HPC-SSL or HPC-SL of '683 into the formulation of '488 with predictable results. A skilled artisan would know how to make such a substitution of one generic HPC of '488 for the specific HPC-SSL or HPC-SL of '683 and would be especially motivated to make such a substitution since '683 teaches that the low viscosity HPC (such as HPC-SSL) is preferred since the binding power is not to high.

Claims 14-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 2003/0060488 ('488) in view of WO 01/82875 ('875) or US 2004/0106660 ('660) and further in view of US 5,547,683 ('683).

- '488 is taught above and teaches a combination of an insulin sensitizer preferably pioglitazone HCl with a HMG-CoA reductase inhibitor like a statin compound such as pravastatin, simvastatin, atorvastatin, etc [0009, 0023, 0025-0026, 0123, 0139, 0145-0148] (according to claims 14 and 18-19). '488 teaches that such a combination is desirable since a lower dose of the pharmaceutical agents can be used for therapeutic results which decreases the amount of unpreferable action of these actives and enhanced preferred activity [0173-0174] (according to the limitations of claims 14 and 20).

'488 does not teach a coating containing pioglitazone HCl over a core containing an active, but does teach that a coating comprising water soluble polymers such hydroxypropylmethylcellulose or hydroxypropylcellulose, etc can be included [0158].

- '875 teaches that the shell layer comprising the pioglitazone HCl is formed via solvent removal process (pg. 7, line 31-pg. 8, line 2) and that cellulosic polymers and polyvinyl alcohol are taught as a biodegradable material further included in the coating of the dosage form (pg. 7, lines 21-27) (according to the limitations of claim 1 and 5-7). '875 teaches that additional actives (a third pharmaceutical) can be added to the core (pg. 3, lines 10-14 or pg. 6, lines 9-11).
- '660 is taught above and teaches a coating is formed via spraying a suspension of comprising the pioglitazone HCl and hydroxypropylmethylcellulose or hydroxypropylcellulose in purified water ([0035, 0023], [0042] table; and Examples 1-2) (according to the limitations of claim 14-17 and 20). '660 teaches that a second active drug can be incorporated into the dosage form with the first active [0034].

'448, '875 or '660 do not teach the specific HPC as instant claimed.

- '683 teaches coating a granule with 5% HPC-SSL (Example 1) and that low viscosity polymers of HPC (such as HPC-SL and HPC-SSL) are preferably used since their binding power is not to high and allows easy control of particles (col. 4, lines 24-33).
- The prior art teaches the same method of coating a dosage form with the same composition as instant claimed and it is therefore assumed in the absence of evidence otherwise to have the same dissolution improvement (as required by the limitation of claim 20).

In view of the combined teachings of the prior art, one of ordinary skill in the art would have been motivated to shift the position of the pioglitazone hydrochloride within the composition from being generally combined with, as practiced by '488, to being dispersed within the coating that surrounds the active core, as practiced by '875 or '660 with a reasonable expectation of manufacturing a coated dosage form capable of delivering dual active ingredients to patients. Such would have been obvious in the absence of evidence to the contrary because '875 or '660 teach that the creation of a formulation where multiple medicaments create a synergistic effect and further '488 teaches that an enhanced effect is observed for the combination of pioglitazone HCl with a HMG-CoA reductase inhibitor [0173-0174]. It is also taught that the '488 actives can be formulated separately and a '488 coated core formulation is known, while '875 or '660 are simply relied upon to teach the technique of placing the second active (or pioglitazone HCl) into the coating. Thus a combination of a known product (i.e. pioglitazone HCl with a HMG-CoA reductase inhibitor) with synergistic effect is known in the art and the known technique of spray drying a coating comprising pioglitazone HCl into a dosage form is also known and such a rearrangement of the second active from within the core to the outer coating is not outside the purview of the skilled artisan. Further, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the low viscosity cellulosic polymer HPC-SSL or HPC-SL of '683 into the formulation of '488, '875, '660 with predictable results. A skilled artisan would know how to make such a substitution of one generic HPC of '488, '875, '660 for the specific HPC-SSL or HPC-SL of '683 and would be especially motivated to

make such a substitution since '683 teaches that the low viscosity HPC (such as HPC-SSL) is preferred since the binding power is not to high.

Response to Arguments

Applicant's arguments with respect to claims 14-20 have been considered but are moot in view of the new grounds of rejection necessitated by applicants' amendments.

Conclusions

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bethany Barham whose telephone number is (571)272-6175. The examiner can normally be reached on M-F, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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